

Listing of Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

1.-49. (Canceled)

50. (Currently amended) A process for the preparation of a rapidly disintegrating solid dosage form capable of forming a stable suspension without irreversible particle aggregation and/or particle agglomeration, or particle growth, comprising the steps of:

- a) preparing an aqueous suspension including a water insoluble or poorly water-soluble drug in the presence of one or more surface stabilizing agents, of which at least one is a phospholipid, wherein the concentration of the phospholipid in the aqueous suspension ~~can~~ range ranges from about 0.1% w/w to about 90% w/w;
- b) subjecting the aqueous suspension to a particle fragmentation process to form a homogeneous aqueous suspension of micron and submicron particles, wherein the mean volume weighted particle size of the water-insoluble or poorly water-soluble drug particles in the suspension ~~can~~ range ranges between about 0.05 and about 10 micrometers;
- c) admixing the homogenous suspension of step b) with [a] one or more rapidly dispersible matrix-forming bulking/releasing ~~agent~~ agents, or a combination of ~~matrix-forming bulking and releasing agents~~ a matrix-forming bulking agent and a matrix-forming releasing agent;
- d) drying the admixture to produce a solid having surface stabilized drug particles dispersed and embedded throughout a support matrix formed by the one or more matrix-forming ~~agent or bulking/releasing agents, or combination thereof~~, wherein the support matrix dissolves or substantially disperses in a rapid disintegration time upon contact between the solid and aqueous environment resulting in a release of the surface stabilized drug particles into the aqueous environment as a suspension ~~without irreversible particle aggregation and/or particle agglomeration and without particle size growth~~; and further wherein, after contact between the solid and the aqueous environment, the resulting suspension comprises no more than about 20% by weight of aggregated or agglomerated primary particles;
- e) optionally course milling and blending the solid with one or more pharmaceutically acceptable excipients to produce a dried powder; and

f) forming the solid or dried powder into a solid dosage form of the drug.

51. (Currently amended) The process [of] according to claim 50, wherein the one or more matrix-forming bulking/releasing ~~agent~~ agents is selected from the group consisting of a pharmaceutically acceptable saccharide, a pharmaceutically acceptable polysaccharide, a pharmaceutically acceptable humectant, a pharmaceutically acceptable cellulose based polymer, combinations thereof, and combinations of these with a pH buffering salt.

52. (Currently amended) The process [of] according to claim 50, wherein the one or more matrix-forming bulking/releasing ~~agent~~ agents is selected from the group consisting of mannitol; trehalose; sorbitol; maltose; and combinations thereof, combinations of mannitol, trehalose, sorbitol and maltose with lactose; combinations of mannitol, trehalose, sorbitol, maltose, and lactose with sucrose; and combinations thereof with a pH buffering salt.

53. (Currently amended) The process [of] according to claim 50, wherein the one or more matrix-forming bulking/releasing ~~agent~~ agents is selected from the group consisting of mannitol; trehalose; sorbitol; and maltose; combinations of mannitol, trehalose, sorbitol, and maltose with lactose; combinations of mannitol, trehalose, sorbitol, maltose, and lactose with sucrose; microcrystalline cellulose; hydroxymethyl cellulose; hydroxypropyl cellulose; methylcellulose; and combinations thereof, and combinations thereof with a pH buffering salt.

54. (Currently amended) The process [of] according to claim 50, wherein the one or more matrix-forming bulking/releasing agents ~~agent~~ is present in an amount between 0.1 % w/w and 90% w/w of the aqueous suspension.

55. (Currently amended) The process [of] according to claim 50, wherein the rapid disintegration time is less than 2 minutes.

56. (Currently amended) The process [of] according to claim 50, wherein the water-insoluble or poorly water-soluble drug is selected from the group consisting of antifungal agents, immunosuppressive agents, immunoactive agents, antiviral agents, antineoplastic agents, analgesic agents, anti-inflammatory agents, antibiotic agents, antiepileptic agents, anesthetic agents, hypnotic agents, sedative agents, antipsychotic agents, neuroleptic agents, antidepressant agents, anxiolytic

agents, anticonvulsant agents, antagonist agents, neuron blocking agents, anticholinergic agents, cholinomimetic agents, antimuscarinic agents, muscarinic agents, anti adrenergic agents, antiarrhythmic agents, antihypertensive agents, hormones, and nutrients.

57. (Currently amended) The process [of] according to claim 50, wherein the drug is selected from the group consisting of fenofibrate, itraconazole, and cyclosporine.

58. (Currently amended) The process [of] according to claim 50, wherein the drug is present in an amount between 0.1 % w/w and 60% w/w of the aqueous suspension.

59. (Currently amended) The process [of] according to claim 50, wherein the phospholipid is selected from the group consisting of an egg phospholipid, a soybean phospholipid, and combinations thereof.

60. (Currently amended) The process [of] according to claim 50, wherein the phospholipid is selected from the group consisting of hydrogenated phospholipid, partially hydrogenated phospholipid, and combinations thereof.

61. (Currently amended) The process [of] according to claim 50, wherein the phospholipid is selected from the group consisting of phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, phosphatidylinositol, phosphatidylglycerol, phosphatidic acid, a lysophospholipid, and combinations thereof.

62. (Currently amended) The process [of] according to claim 50, wherein the surface ~~modifier~~ stabilizing agent is selected from the group consisting of pharmaceutically acceptable nonionic surfactants, pharmaceutically acceptable anionic surfactants, and pharmaceutically acceptable cationic surfactants.

63. (Currently amended) The process [of] according to claim 50, wherein the surface ~~modifier~~ stabilizing agent is selected from the group consisting of casein, gelatin, tragacanth, acacia, and combinations thereof.

64. (Currently amended) The process [of] according to claim 50, wherein the surface ~~modifier~~ stabilizing agent is selected from the group consisting of a pharmaceutically acceptable

polyoxyethylene fatty alcohol ether, a sorbitan fatty acid ester, a polyoxyethylene fatty acid ester, a poloxamer, a polaxamine, and combinations thereof.

65. (Currently amended) The process [of] according to claim 50, wherein the surface ~~modifier~~ stabilizing agent is selected from the group consisting of glycerol monostearate, cetyl alcohol, cetostearyl alcohol, stearyl alcohol, and combinations thereof.

66. (Currently amended) The process [of] according to claim 50, wherein the surface ~~modifier~~ stabilizing agent is selected from the group consisting of potassium laurate, triethanolamine stearate, sodium lauryl sulfate, an alkyl polyoxyethylene sulfate, sodium alginate, sodium deoxycholate, dioctyl sodium sulfosuccinate, a negatively charged glyceryl ester, sodium carboxymethylcellulose, calcium carboxymethylcellulose, and combinations thereof.

67. (Currently amended) The process [of] according to claim 50, wherein the surface ~~modifier~~ stabilizing agent is selected from the group consisting of benzalkonium chloride, cetyltrimethylammonium bromide, lauryldimethylbenzylammonium chloride, and combinations thereof.

68. (Currently amended) The process [of] according to claim 50, wherein the surface ~~modifier~~ stabilizing agent is present in an amount between 0.5% w/w and 50% w/w of the aqueous suspension.

69. (Currently amended) The process [of] according to claim 50, wherein the admixture is dried by spray drying, spray coating, or freeze-drying.

70. (Currently amended) The process [of] according to claim 50, wherein the particle fragmentation process is selected from the group consisting of sonication, milling, homogenization, microfluidization, [and] antisolvent precipitation and solvent precipitation.

71. (Currently amended) The process [of] according to claim 50, wherein the pharmaceutically acceptable excipient is a tableting aid for compression, a glidant for hard gelatin encapsulation, aneffervescent disintegration agent, a dispersant for a dry powder inhaler, or a combination thereof.

72. (Currently amended) The process [of] according to claim 50, wherein the dosage form is a tablet, a gelatin encapsulation, or a powder.

73. (Currently Amended) A process for the preparation of a rapidly disintegrating solid dosage form capable of forming a stable suspension without irreversible particle aggregation and/or particle agglomeration or particle growth comprising the steps of:

a) admixing a matrix-forming bulking/releasing agent or a combination of matrix-forming bulking and releasing agents with an aqueous homogeneous suspension including solid drug particles onto which is adsorbed at least one surface ~~modifying~~ stabilizing agent of which one is a phospholipid, wherein the aqueous homogeneous suspension ~~having been~~ is prepared with a water insoluble or poorly water-soluble drug in the presence of one or more surface stabilizing agents, of which at least one is a phospholipid and is subjected to a particle fragmentation process resulting in a suspension of micron and submicron particles, wherein the mean volume weighted particle size of the water-insoluble or poorly water-soluble drug particles in the suspension ~~can range~~ ranges between about 0.05 and about 10 micrometers;

b) distributing the admixture of step (a) into unit dosage form molds; and

c) freeze-drying said admixture in said unit dosage form molds to produce a solid dosage form of the surface stabilized drug particles dispersed and embedded throughout a support matrix of said matrix-forming agent or agents, wherein said matrix dissolves or substantially disperses in a rapid disintegration time upon contact with an aqueous environment to release the surface stabilized drug particles into the aqueous environment as a suspension ~~without irreversible particle aggregation and/or particle agglomeration and without particle size growth~~; and further after contact between the solid and the aqueous environment, the resulting suspension comprises no more than 20% by weight of aggregated or agglomerated primary particles.

74. (Currently amended) The process [of] according to claim 73, wherein the matrix-forming bulking/releasing agent is selected from the group consisting of a pharmaceutically acceptable saccharide, a pharmaceutically acceptable polysaccharide; a pharmaceutically acceptable humectant a pharmaceutically acceptable cellulose based polymer, combinations thereof, and combinations of these with a pH buffering salt.

75. (Currently amended) The process [of] according to claim 73, wherein the matrix-forming bulking/releasing agent is selected from the group consisting of mannitol; trehalose; sorbitol; maltose; and combinations thereof, combinations of mannitol, trehalose, sorbitol, and maltose with

lactose; combinations of mannitol, trehalose, sorbitol, maltose, and lactose with sucrose; and combinations thereof with a pH buffering salt.

76. (Currently amended) The process [of] according to claim 73, wherein the matrix-forming bulking/releasing agent is selected from the group consisting of mannitol; trehalose; sorbitol; and maltose; combinations of mannitol, trehalose, sorbitol and maltose with lactose; combinations of mannitol, trehalose, sorbitol, maltose, and lactose with sucrose; microcrystalline cellulose; hydroxymethyl cellulose; hydroxypropyl cellulose; methylcellulose; combinations thereof, and combinations thereof with a pH buffering salt.

77. (Currently amended) The process [of] according to claim 73, wherein the matrix-forming bulking/releasing agent is present in an amount between 0.1 % w/w and 90% w/w of the aqueous suspension.

78. (Currently amended) The process [of] according to claim 73, wherein the rapid disintegration time is less than 2 minutes.

79. (Currently amended) The process [of] according to claim 73, wherein the water insoluble or poorly water-soluble drug is selected from the group consisting of antifungal agents, immunosuppressive agents, immunoactive agents, antiviral agents, antineoplastic agents, analgesic agents, anti-inflammatory agents, antibiotic agents, antiepileptic agents, anesthetic agents, hypnotic agents, sedative agents, antipsychotic agents, neuroleptic agents, antidepressant agents, anxiolytic agents, anticonvulsant agents, antagonist agents, neuron blocking agents, anticholinergic agents, cholinomimetic agents, antimuscarinic agents, muscarinic agents, anti adrenergic agents, antiarrhythmic agents, antihypertensive agents, hormones, and nutrients.

80. (Currently amended) The process [of] according to claim 73, wherein the drug is fenofibrate, itraconazole, or cyclosporine.

81. (Currently amended) The process [of] according to claim 73, wherein the drug is present in an amount between 0.1 % w/w and 60% w/w of the aqueous suspension.

82. (Currently amended) The process [of] according to claim 73, wherein the phospholipid is selected from the group consisting of an egg phospholipid, a soybean phospholipid, and combinations thereof.

83. (Currently amended) The process [of] according to claim 73, wherein the phospholipid is selected from the group consisting of hydrogenated phospholipid, partially hydrogenated phospholipid, and combinations thereof.

84. (Currently amended) The process [of] according to claim 73, wherein the phospholipid is selected from the group consisting of phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, phosphatidylinositol, phosphatidylglycerol, phosphatidic acid, a lysophospholipid, and combinations thereof.

85. (Currently amended) The process [of] according to claim 73, wherein the surface ~~modifier~~ modifying agent is selected from the group consisting of pharmaceutically acceptable nonionic surfactants, pharmaceutically acceptable anionic surfactants, and pharmaceutically acceptable cationic surfactants.

86. (Currently amended) The process [of] according to claim 73, wherein the surface ~~modifier~~ modifying agent is selected from the group consisting of casein, gelatin, tragacanth, acacia, and combinations thereof.

87. (Currently amended) The process [of] according to claim 73, wherein the surface ~~modifier~~ modifying agent is selected from the group consisting of a pharmaceutically acceptable polyoxyethylene fatty alcohol ether, a sorbitan fatty acid ester, a polyoxyethylene fatty acid ester, a poloxamer, a polaxamine, and combinations thereof.

88. (Currently amended) The process [of] according to claim 73, wherein the surface ~~modifier~~ modifying agent is selected from the group consisting of glycerol monostearate, cetyl alcohol, cetostearyl alcohol, stearyl alcohol, and combinations thereof.

89. (Currently amended) The process [of] according to claim 73, wherein the surface ~~modifier~~ modifying agent is selected from the group consisting of potassium laurate, triethanolamine stearate,

sodium lauryl sulfate, an alkyl polyoxyethylene sulfate, sodium alginate, sodium deoxycholate, dioctyl sodium sulfosuccinate, a negatively charged glyceryl ester, sodium carboxymethylcellulose, calcium carboxymethylcellulose, and combinations thereof.

90. (Currently amended) The process [of] according to claim 73, wherein the surface ~~modifier~~ modifying agent is selected from the group consisting of benzalkonium chloride, cetyltrimethylammonium bromide, lauryldimethylbenzylammonium chloride, and combinations thereof.

91. (Currently amended) The process [of] according to claim 73, wherein the surface ~~modifier~~ modifying agent is present in an amount between 0.5% w/w and 50% w/w of the aqueous suspension.

92. (Currently amended) The process [of] according to claim 73, wherein the particle fragmentation process is selected from the group consisting of sonication, milling, homogenization, microfluidization, ~~and~~ antisolvent precipitation and solvent precipitation.

93. (Currently amended) The process [of] according to claim 73, wherein the dosage form is a tablet.

94. (Original) A dosage form prepared by the process of claim 50.

95. (Original) A dosage form prepared by the process of claim 73.

96. (Canceled)

97. (New) A process for the preparation of a rapidly disintegrating solid dosage form capable of forming a stable suspension without irreversible particle aggregation and/or particle agglomeration, or particle growth, comprising the steps of:

a) preparing an aqueous suspension including a water insoluble or poorly water-soluble drug in the presence of one or more surface stabilizing agents, of which at least one is a phospholipid, wherein the concentration of the phospholipid in the aqueous suspension ranges from about 0.1% w/w to about 90% w/w;

b) admixing the aqueous suspension of step a) with one or more rapidly dispersible matrix-forming bulking/releasing agents, or a combination of a matrix-forming bulking agent and a matrix-forming releasing agent;

c) subjecting the aqueous suspension to a particle fragmentation process to form a homogeneous aqueous suspension of micron and submicron particles, wherein the mean volume weighted particle size of the water-insoluble or poorly water-soluble drug particles in the suspension ranges between about 0.05 and about 10 micrometers;

d) drying the homogeneous suspension of step c) to produce a solid having surface stabilized drug particles dispersed and embedded throughout a support matrix formed by the one or more matrix-forming bulking/releasing agents, or combination thereof;

wherein the support matrix dissolves or substantially disperses in a rapid disintegration time upon contact between the solid and aqueous environment resulting in a release of the surface stabilized drug particles into the aqueous environment as a suspension; and further wherein, after contact between the solid and the aqueous environment, the resulting suspension comprises no more than 20% by weight of aggregated or agglomerated primary particles;

e) optionally coarse milling and blending the solid with one or more pharmaceutically acceptable excipients to produce a dried powder; and

f) forming the solid or dried powder into a solid dosage form of the drug.

98. (New) A process for the preparation of a rapidly disintegrating solid dosage form capable of forming a stable suspension without irreversible particle aggregation and/or particle agglomeration, or particle growth, comprising the steps of:

a) preparing an aqueous suspension including a water insoluble or poorly water-soluble drug selected from the group consisting of cyclosporine, itraconazole and fenofibrate, in the presence of one or more surface stabilizing agents selected from the group consisting of Myrj™ 52, polyvinyl pyrrolidone (PVP 17), sodium deoxycholate, TWEEN™ 80 and a combination thereof, and further including at least one phospholipid selected from the group consisting of phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, phosphatidylinositol, phosphatidylglycerol, phosphatidic acid, a lysophospholipid, and combinations thereof; wherein the concentration of the phospholipid in the aqueous suspension ranges from about 0.1% w/w to about 90% w/w;

b) subjecting the aqueous suspension of step a) to a particle fragmentation process to form a homogeneous aqueous suspension of micron and submicron particles, wherein the mean volume weighted particle size of the water-insoluble or poorly water-soluble drug particles in the suspension ranges between about 0.05 and about 10 micrometers;

c) admixing the homogenous suspension of step b) with one or more rapidly dispersible matrix-forming bulking/releasing agents, or a combination of a matrix-forming bulking agent and a matrix-forming releasing agent, said one or more bulking/releasing agents selected from the group consisting of sucrose, lactose, trehalose, mannitol, sorbitol and a combination thereof;

d) drying the admixture to produce a solid having surface stabilized drug particles dispersed and embedded throughout a support matrix formed by the one or more matrix-forming bulking/releasing agents, or combination thereof;

wherein the support matrix dissolves or substantially disperses in a rapid disintegration time upon contact between the solid and aqueous environment resulting in a release of the surface stabilized drug particles into the aqueous environment as a suspension; and further wherein, after contact between the solid and the aqueous environment, the resulting suspension comprises no more than 20% by weight of aggregated or agglomerated primary particles;

e) optionally course milling and blending the solid with one or more pharmaceutically acceptable excipients to produce a dried powder; and

f) forming the solid or dried powder into a solid dosage form of the drug.

99. (New) The method according to any one of claims 50, 73, 97, or 98, wherein, in step d), said reconstituted suspension comprises no more than 10% by weight of aggregated primary particles.

100. (New) The method according to any one of claims 50, 73, 97, or 98, wherein, in step d), said reconstituted suspension comprises no more than 1% by weight of aggregated primary particles.

101. (New) A dosage form prepared by the process of claim 97.

102. (New) A dosage form prepared by the process of claim 98.

103. (New) The process according to claim 97, wherein the one or more matrix-forming bulking/releasing agents is selected from the group consisting of a pharmaceutically acceptable saccharide, a pharmaceutically acceptable polysaccharide, a pharmaceutically acceptable humectant, a pharmaceutically acceptable cellulose based polymer, combinations thereof, and combinations of these with a pH buffering salt.

104. (New) The process according to claim 97, wherein the one or more matrix-forming bulking/releasing agents is selected from the group consisting of mannitol; trehalose; sorbitol; maltose; and combinations thereof, combinations of mannitol, trehalose, sorbitol and maltose with lactose; combinations of mannitol, trehalose, sorbitol, maltose, and lactose with sucrose; and combinations thereof with a pH buffering salt.

105. (New) The process according to claim 97, wherein the one or more matrix-forming bulking/releasing agents is selected from the group consisting of mannitol; trehalose; sorbitol; and maltose; combinations of mannitol, trehalose, sorbitol, and maltose with lactose; combinations of mannitol, trehalose, sorbitol, maltose, and lactose with sucrose; microcrystalline cellulose; hydroxymethyl cellulose; hydroxypropyl cellulose; methylcellulose; and combinations thereof, and combinations thereof with a pH buffering salt.

106. (New) The process according to claim 97 or claim 98, wherein the one or more matrix-forming bulking/releasing agent is present in an amount between 0.1 % w/w and 90% w/w of the aqueous suspension.

107. (New) The process according to claim 97 or claim 98, wherein the rapid disintegration time is less than 2 minutes.

108. (New) The process according to claim 97, wherein the water-insoluble or poorly water-soluble drug is selected from the group consisting of antifungal agents, immunosuppressive agents, immunoactive agents, antiviral agents, antineoplastic agents, analgesic agents, anti-inflammatory agents, antibiotic agents, antiepileptic agents, anesthetic agents, hypnotic agents, sedative agents, antipsychotic agents, neuroleptic agents, antidepressant agents, anxiolytic agents, anticonvulsant agents, antagonist agents, neuron blocking agents, anticholinergic agents, cholinomimetic agents,

antimuscarinic agents, muscarinic agents, anti adrenergic agents, antiarrhythmic agents, antihypertensive agents, hormones, and nutrients.

109. (New) The process according to claim 97, wherein the drug is selected from the group consisting of fenofibrate, itraconazole, and cyclosporine.

110. (New) The process according to claim 97 or claim 98, wherein the drug is present in an amount between 0.1 % w/w and 60% w/w of the aqueous suspension.

111. (New) The process according to claim 97, wherein the phospholipid is selected from the group consisting of an egg phospholipid, a soybean phospholipid, and combinations thereof.

112. (New) The process according to claim 97, wherein the phospholipid is selected from the group consisting of hydrogenated phospholipid, partially hydrogenated phospholipid, and combinations thereof.

113. (New) The process according to claim 97, wherein the phospholipid is selected from the group consisting of phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, phosphatidylinositol, phosphatidylglycerol, phosphatidic acid, a lysophospholipid, and combinations thereof.

114. (New) The process according to claim 97, wherein the surface stabilizing agent is selected from the group consisting of pharmaceutically acceptable nonionic surfactants, pharmaceutically acceptable anionic surfactants, and pharmaceutically acceptable cationic surfactants.

115. (New) The process according to claim 97, wherein the surface stabilizing agent is selected from the group consisting of casein, gelatin, tragacanth, acacia, and combinations thereof.

116. (New) The process according to claim 97, wherein the surface stabilizing agent is selected from the group consisting of a pharmaceutically acceptable polyoxyethylene fatty alcohol ether, a sorbitan fatty acid ester, a polyoxyethylene fatty acid ester, a poloxamer, a poloxamine, and combinations thereof.

117. (New) The process according to claim 97, wherein the surface stabilizing agent is selected from the group consisting of glycerol monostearate, cetyl alcohol, cetostearyl alcohol, stearyl alcohol, and combinations thereof.

118. (New) The process according to claim 97, wherein the surface stabilizing agent is selected from the group consisting of potassium laurate, triethanolamine stearate, sodium lauryl sulfate, an alkyl polyoxyethylene sulfate, sodium alginate, sodium deoxycholate, dioctyl sodium sulfosuccinate, a negatively charged glyceryl ester, sodium carboxymethylcellulose, calcium carboxymethylcellulose, and combinations thereof.

119. (New) The process according to claim 97, wherein the surface stabilizing agent is selected from the group consisting of benzalkonium chloride, cetyltrimethylammonium bromide, lauryldimethylbenzylammonium chloride, and combinations thereof.

120. (New) The process according to claim 97, wherein the surface stabilizing agent is present in an amount between 0.5% w/w and 50% w/w of the aqueous suspension.

121. (New) The process according to claim 97 or claim 98, wherein, in step d), the admixture is dried by spray drying, spray coating, or freeze-drying.

122. (New) The process according to claim 97 or claim 98, wherein the particle fragmentation process is selected from the group consisting of sonication, milling, homogenization, microfluidization, antisolvent precipitation and solvent precipitation.

123. (New) The process according to claim 97 or claim 98, wherein the pharmaceutically acceptable excipient is a tableting aid for compression, a glidant for hard gelatin encapsulation, aneffervescent disintegration agent, a dispersant for a dry powder inhaler, or a combination thereof.

124. (New) The process according to claim 97 or claim 98, wherein the dosage form is a tablet, a gelatin encapsulation, or a powder.